Methyl O-methyl-N-(benzyl)phosphonamidothionate (**6a**): (58% yield); mp = 55°C. ^{1}H-NMR ($CDCl_3$): δ 1.7 (3H, d, J = 14.5 Hz), 3.2 (1H, br s), 3.54 (3H, d, J = 14.0 Hz), 4.18 (2H, dq, J = 15, 7 Hz), 7.27 (5H, s); ^{13}C-NMR ($CDCl_3$) δ 20.3 (d, J = 107.0 Hz), 45.5, 50.4 (d, J = 6 Hz), 127.1, 127.3, 128.5, 139.0 (d, J = 6.5 Hz); ^{31}P-NMR ($CDCl_3$) δ 85.4. Anal. Calc. for $C_9H_{14}NOPS$: C, 50.2; H, 6.61; N, 6.51. Found: C, 50.31; H, 6.42; N, 6.43.

Methyl O-methyl-N-(p-methoxybenzyl)phosphonamidothionate (**6b**): (65% yield); ^{1}H NMR ($CDCl_3$): δ 1.78 (3H, d, *J* = 14.0 Hz), 3.3 (1H, br), 3.57 (3H, d, *J* = 14.0 Hz), 3.80 (3H, s), 4.18 (2H, m), 6.87 (2H, d, *J* = 8.2 Hz), 7.22 (2H, d, *J* = 8.2 Hz); ^{13}C NMR($CDCl_3$): 20.35 (d, *J* = 128.2 Hz), 45.2, 50.4, 50.5, 113.9, 128.6, 131.1, 158.0; ^{31}P NMR ($CDCl_3$): δ 85.8. Anal. Calc. for $C_{10}H_{16}NPO_2S$: C, 48.96; H, 6.57; N, 5.71. Found: C, 48.89; H, 6.52; N, 5.66.

Methyl O-methyl-N-(methyl)-N-(benzyl)phosphonamidothionate (**6c**): (43% yield); mp = 68°C. ^{1}H-NMR ($CDCl_3$): δ 1.43 (3H, d, J = 16.0 Hz), 2.43 (2H, d, J = 9.6 Hz), 3.57 (3H, d, J = 11.2 Hz), 4.17 (2H, d, J = 8.0 Hz), 7.30 (5H, s); ^{13}C-NMR ($CDCl_3$): δ 10.6 (d, J = 133.0 Hz), 32.0, 49.5, 51.6, 126.9, 127.6, 128.0, 136.5: ^{31}P-NMR ($CDCl_3$): δ 83.9. Anal. Calc. for: $C_{10}H_{16}NPOS$: C, 52.3; H, 7.04; N, 6.11. Found: C, 52.14; H, 6.86; N, 6.11.

General procedure for the titration of phosphorus acids 1-3: A 0.0422 M solution of compound **1, 2** or **3** (0.422 mmol) was prepared in 10.0 mL of distilled water. The pH of the solution was closely monitored while 0.5 mL aliquots of a normalized NaOH solution (0.0500 N) were added with constant stirring. After 15.0 mL of NaOH was added and the pH value of the solution remained constant, the titration was halted. The observed pH versus the volume of NaOH was plotted and the pKa value was obtained at half of the equilibrium point. The titration of each compound was repeated six times and the mean and standard deviation calculated. The pKa values were compared to values for benzoic and acetic acid and corrected for any deviation from the literature values.

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Photoinduced Molecular Transformations. Part 159.[1] Formation of Some Furonaphthyridinones by Selective β-Scission of Cyclobutanoxyl Radicals Generated From [2+2] Photoadducts of 4-Hydroxy-1-phenyl [1,8] naphthyridin-2(1*H*)-one with Alkenes

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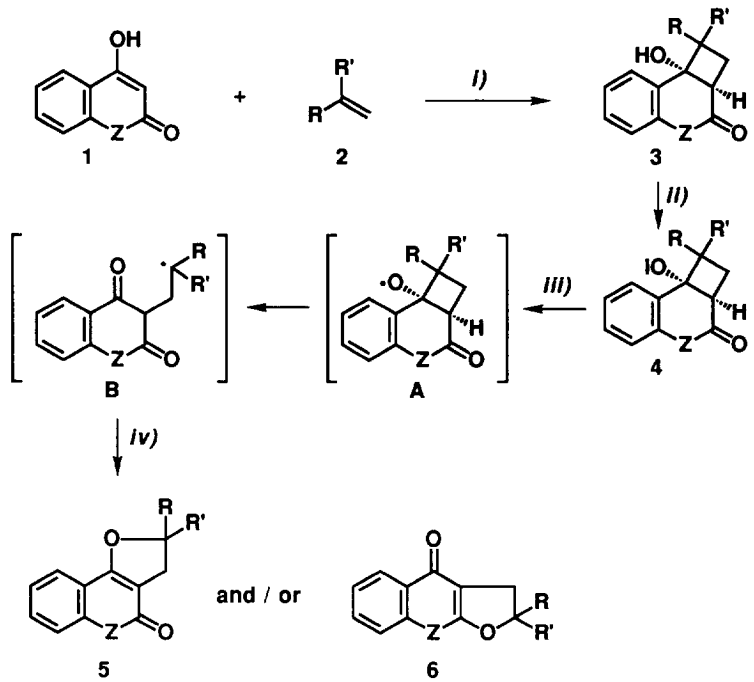
Abstracts: The [2+2] photoaddition of 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1*H*)-one **7** with various alkenes in methanol gave regioselectively the corresponding *head-to-tail* adducts (**8,9,** and**11**). The photolysis of the hypoiodites generated by the *in situ* reaction of the cyclobutanol adducts **8,9,** and **11** with excess mercury(II) oxide-iodine reagent in benzene induced a regioselective scission of their non-ring junction bond of the corresponding alkoxyl radicals to give substituted 3,9-dihydro-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one (**12** and **15**) and/or substituted 3,5-dihydro-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4-(2*H*)-one (**13,14,** and **16**). An unusual byproduct **12a** was formed in the photolysis of the hypoiodite of the [2+2] photoadduct **8a** of 4-hydroxy-1-phenyl [1,8]naphthyridin-2-(1*H*)-one with isobutene. Copyright © 1996 Elsevier Science Ltd

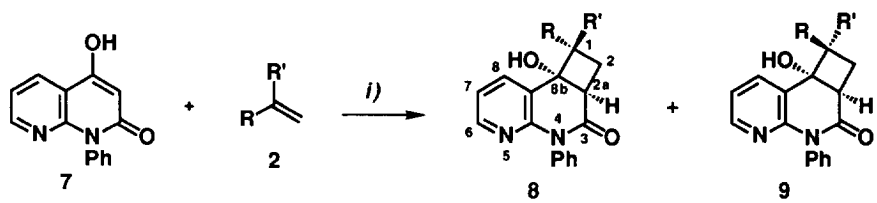
We have shown that a variety of molecules, including natural products, can be synthesized using the β-scission of alkoxyl radicals, generated by the photolysis of hypoiodites of appropriate alcohols or lactols, as the key step.[2] As part of the investigations we have reported on a new radical process by which a hydroxyl oxygen of a fused cyclobutanol is incorporated into the cyclobutane to give a fused furan.[3] The reaction was found to be useful for attaching a furan ring to some heteroaromatics, such as coumarin and 2-quinolinone, by combining the process with a [2+2] photoaddition with alkenes.[3] Thus, several furoheteroaromatics have been prepared *via* the following two principal processes: (i) the [2+2] photoaddition of heteroaromatics, such as 3- or 4-hydroxycoumarin **1** (Z=O),[3a,c] 4-hydroxyquinolin-2(1*H*)-one **1** (Z=NMe),[3b] and 4-hydroxyisoquinolin-1-(2*H*)-one,[3d] with alkenes **2** to give the cyclobutanols **3;** (ii) a regioselective β-scission of the alkoxyl radicals **A** generated from the cyclobutanols by the photolysis of the corresponding hypoiodites **4** (prepared by an *in situ* reaction of the cyclobutanols **3** with mercury(II) oxide-iodine reagent) and a spontaneous recyclization of the resulting carbon-centred radical **B** to give furanoheterocycles (**5** and/or **6**), as outlined in Scheme 1.[3]



Reagents and Conditions ;
I) hν ; *II)* HgO, I_2 ; *III)* hν ; *IV)* -e, $-H^+$

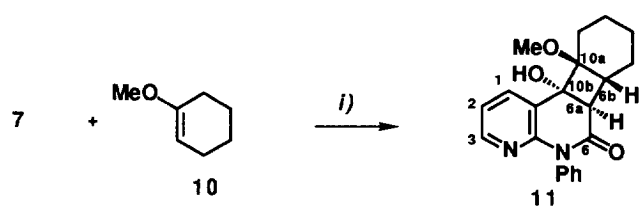
Z = O or NMe,
R = R' = H, alkyl, alkoxyl, acetoxy etc.

Scheme 1



a ; R = R' = Me ; b ; R = OEt, R' = H ; c ; R = OAc, R' = Me

Scheme 2 ***Reagents and Conditions*** ; *I)* hν, MeOH



Scheme 3 ***Reagents and Conditions*** ; *I)* hν, MeOH

In order to further examine the substrate-product relationship of this new reaction and to develop the synthetic potential of this transformation we have extended the annulation to [1,8]naphthyridin-2(1*H*)-one, and we report here the results in full.

A number of derivatives of the furonaphthyridines have been prepared from the viewpoint of their pharmacological activity.[4]

RESULTS

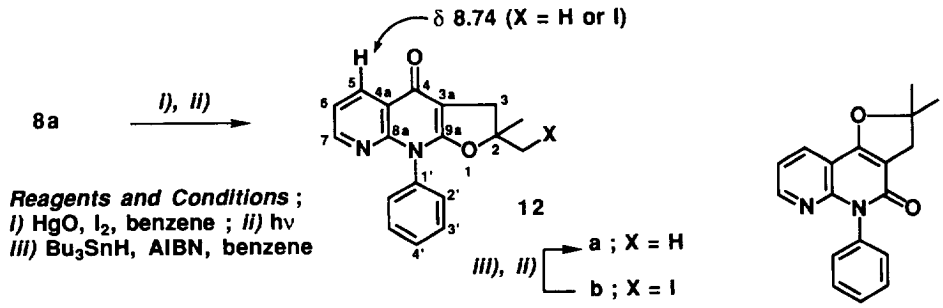
Preparations of Cyclobutanols **8a-c, 9b, c** *and* **11** *by the* [2+2] *Photoaddition of* 4-*Hydroxyphenyl* [1,8] *naphthyridin*-2(1H)-*one* **7** *with Isobutene* **2a,** *Ethyl Vinyl Ether* **2b,** *Isopropenyl Acetate* **2c,** *and* 1-*Methoxy*-1-*cyclohexene* **10** *(Schemes* 2 *and* 3*).* —— The irradiation of 4-hydroxy-1-phenyl [1,8] naphthyridin-2(1*H*)-one **7**[5] with an excess amount of isobutene **2a** in methanol for 15h with Pyrex-filtered light gave an exclusive photoadduct **8a** in 95% yield (Scheme 2). The structure was established to be (2aα,8bα)-(±)-2,2a,4,8b-tetrahydro-8b-hydroxy-1,1-dimethyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8a** on the basis of an analysis of the ^{1}H NMR spectrum. The presence of a signal at δ 3.58 (dd) assignable to C(2a)-H indicated that the *gem*-dimethyl groups are attached to C(1), and that product **8a** is a head-to-tail adduct. The cyclobutane and 6-membered ring should be more stable *cis*-fused on steric grounds, since the cycloadduct was stable for a base.

The photoaddition of naphthyridinone **7** with vinyl ether **2b** under similar conditions gave a pair of head-to-tail cycloadducts, **8b** and **9b**, in 37 and 43% yields (Scheme 2). The ^{1}H NMR spectra indicated that they are stereoisomers with respect to the C(1) substituents; their 2a-H appeared as a multiplet at δ 3.58 and a doublet of a doublet at δ 3.03, respectively. The 4/6 rings of cycloadducts **8b** and **9b** should also be *cis*-fused, since they were stable for a base. The NOE measurements indicated that the 2a-H and ethoxyl group attached to C(1) of product **9b** are *cis* oriented; the irradiation of a signal at δ 3.03 resulted in an enhancement of the signal areas at δ 4.14 (dd) and δ 2.52 (ddd) assignable to 1a-H and 2a-H, while irradiation of the signal at δ 4.14 caused an enhancement of the signal areas at δ 3.03 and 2.52.

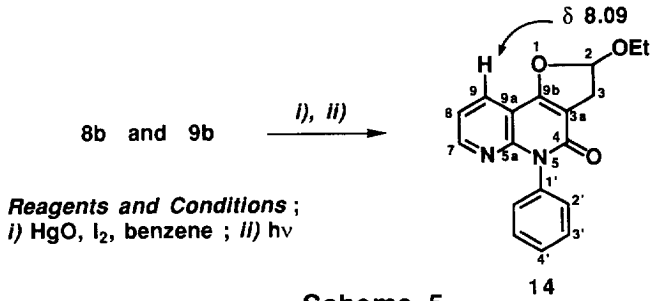
In contrast, the photoaddition of naphthyridinone **7** with isopropenyl acetate **2c** under conditions similar to the above gave a single head-to-tail photoadduct in 76.6% yield (Scheme 2). The ^{1}H NMR spectrum indicated that the OAc and Me substituents were attached to C(1), since a signal at δ 3.25 attributable to C(2a)-H appeared as a doublet of a doublet. However, whether the structure was **8c** or **9c** remained undefined.

Finally, the photoaddition of naphthyridinone **7** with 1-methoxy-1-cyclohexene **10**[6] gave a cyclobutanol **11** as the major photoadduct, (as outlined in Scheme 3). The ^{1}H NMR spectrum exhibited a doublet at δ 3.03 (*J* 10.56) attributable to 6a-H. These NMR spectral data indicated that the cyclobutanol **11** was *cis-transoid-cis* isomer by comparing it with those of 6a-H of (6aα,6bβ,10aβ,10bα)-(±)-6a,6b,7,8,9,10,10a,10b-octahydro-10b-acetoxy-5-methylbenzo[3,4]cyclobuta[1,2-*c*]quinolin-6(5*H*)-one, [obtained by the cycloaddition of 4-acetoxyquinolin-2(1*H*)-one with cyclohexene], the structure of which was determined by an x-ray crystallographic analysis[3b], and its *cis-cisoid-cis* isomer.[3b]

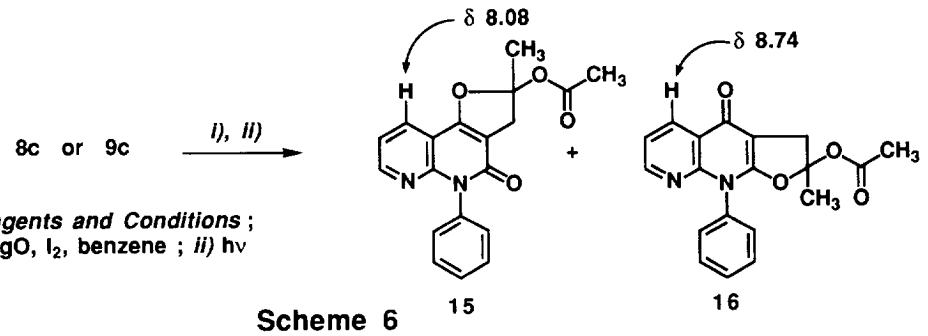
Formation of Furo [2,3-b] *and* [3,2-c][1,8]*naphthyridin*-4-(2H)-*ones* via *β-Scission of Cyclobutanoxyl Radicals Generated from the Photoadducts (Schemes* 4-7)——The irradiation of cyclobutanol **8a** in benzene



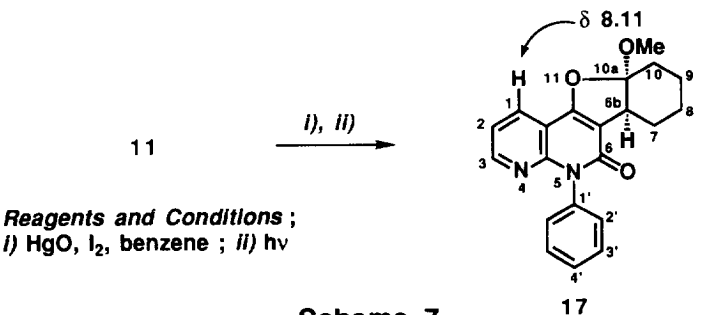
Scheme 4



Scheme 5



Scheme 6



Scheme 7

Table 1 ^{13}C and 2-D NMR data for product 12a

Carbon atom[a]	δ_c / ppm[b]	DEPT	^1H-^{13}C COSY Correlation (δ_H)[b]
C-2	92.5	C	
C-3	39.2	CH_2	3.13
C-3a	99.7	C	
C-4	173.7	C	
C-4a	135.1	C	
C-5	135.2	CH	8.74
C-6	119.5	CH	7.26-7.36
C-7	150.6	CH	8.50
C-8a	161.2	C	
C-9a	120.7	C	
C-2-CH_3	28.1	CH_3	1.52
C-1'	149.9	C	
C-2'	129.2	CH	7.26-7.36
C-3'	129.0		7.52-7.61
C-4'	128.8		

a ; The numbering used here is as shown in the structure in Scheme 4.
b ; δ_c and δ_H values in $CDCl_3$.

Table 2 ^{13}C and 2-D NMR data for product 15

Carbon atom[a]	δ_c / ppm[b]	DEPT	^1H-^{13}C COSY Correlation (δ_H)[b]
C-2	109.3	C	
C-3	40.1	CH_2	3.30, 3.43
C-3a	107.4	C	
C-4	160.9	C	
C-5a	159.6	C	
C-7	150.8	CH	8.47
C-8	117.8	CH	7.15
C-9	131.2	CH	8.08
C-9a	114.7	C	
C-9b	151.7	C	
C-1'	137.2	C	
C-2'	129.4, 129.2	CH[c]	7.24-7.26
C-3'	129.1, 128.4		7.44-7.58
C-4'			
$COCH_3$	168.5, 21.9	C, CH_3	2.10
CH_3	26.0	CH_3	1.99

a ; The numbering used here is as shown in the structure in Scheme 6.
b ; δ_c and δ_H values in $CDCl_3$.
c ; Two of the signals are due to non-equivalent *ortho*-carbons.

containing mercury(II) oxide and iodine (each 3 equiv.) with a 100-W high-pressure Hg arc through a Pyrex-filter for 5h at room temperature gave two products, **12a** and **12b**, in 25.3 and 48.3% yield, as outlined in Scheme 4. A combustion analysis and mass spectrometry of the products indicated that they had the molecular formulae $C_{18}H_{16}N_2O_2$ and $C_{18}H_{15}N_2O_2I$, respectively. The IR spectrum of the product **12a** showed the presence of the enone group of [1,8]naphthyridin-2(1*H*)-one and the absence of a hydroxyl group. The signals due to a proton adjacent to a carbonyl group were lost in the ^1H NMR spectrum. These spectral results in conjunction with the formation paths indicated that the structure was either 3,9-dihydro-2,2-dimethyl-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one **12a** or its angular isomer **13**.

The structure of the product as a linear-type isomer **12a** was established on the basis of IR, ^1H NMR, ^{13}C NMR, and ^1H-^{13}C COSY spectral evidence; the IR spectrum exhibited two intense bands at 1623 and 1591 cm^{-1} assignable to the enone group. A comparison of the band positions of the 2,3-furo-4-quinolinones (linear-type) and 3,4-furo-2-quinolinones (angular-type) showed it to be 2,3-furo-4-naphthyridinone **12a.** The linear isomer was also distinguishable from the corresponding angular isomer by the ^1H NMR spectra. The aromatic proton (5-H) at the peri-position of the former thus appeared at δ 8.7, while the corresponding proton of the latter appeared at δ 8.1. The ^{13}C NMR spectral data are given in Table 1. The assignments of the signals are based on a distortionless enhancement by a polarization transfer (DEPT) and the 2D homonuclear chemical shift correlation (COSY) spectra. The signals due to the conjugated carbonyl carbon and aromatic C(5) appeared at δ 173.7 and 135.2, 12.3, and 3.6 ppm downfield of the corresponding signals of the angular-type isomer **15** (*vide infra*).

The key features of the IR and ^1H NMR spectra of product **12b** were the same as those of product **12a:** the IR spectrum exhibited two intense bands at 1611 and 1592 cm^{-1}. The ^1H NMR spectrum exhibited a signal at δ 8.74 assignable to 5-H. These results indicated that the product had a linear-type structure. In addition to these features, the ^1H NMR spectrum of product **12b** exhibited a pair of doublet signals at δ 3.42 and 3.48 (*J* 10.88 Hz) assignable to non-equivalent methylene protons attached to a carbon having an iodine. These spectral results in conjunction with the formation mechanism (*vide infra*) suggested that the structure of product **12b** was 3,9-dihydro-2-iodomethyl-2-methylphenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one. This structure was then confirmed by transforming it into product **12a** by removing the halogen with Bu_3SnH-AIBN.

The photoreactions of either cyclobutanol **8b** or **9b** under conditions similar to those mentioned above gave the same product **14** in the same 38% yield (Scheme 5). The molecular formula of product **14** was determined to be $C_{18}H_{16}N_2O_3$ by combustion analysis and mass spectrometry. The following spectral analysis indicated that the product **14** was 2-ethoxy-3,5-dihydro-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one arising from the insertion of a hydroxyl oxygen to the cyclobutane ring; the IR spectrum exhibited intense bands at 1667 and 1589 cm^{-1} assignable to the enone group. The band position was parallel to those of unsaturated lactam groups of 3,4-furo-2-quinolinones (linear-type). In the ^1H NMR spectrum, a diagnostic aromatic proton (9-H) at the peri-position on the fused pyridine ring appeared at δ 8.09, *ca.* 0.6 ppm upfield of the signals of the corresponding protons of products, **12a** and **12b.**

While the β-scission of cyclobutanols **8b** and **9b** led to the same single product, the photoreaction of cyclobutanol **8c** or **9c** under the similar conditions gave a pair of products, **15** and **16** in 31 and 21% yield (Scheme 6). A combustion analysis and high-resolution mass spectrometry showed that products **15** and **16** were isomers having the molecular formula $C_{19}H_{16}N_2O_4$. The structures of these products, **15** and **16,** were

confirmed to be 2-acetoxy-3,5-dihydro-2-methyl-5-phenylfuro[3,2-*c*][1,8]naphthyridin-4(2*H*)-one and its linear fused isomer on the basis of their IR, ^{1}H NMR,^{13}C NMR, and ^{1}H-^{13}C COSY spectra and the formation mechanism. The IR spectrum of **15** exhibited an intense band at 1675 and 1590 cm^{-1} assignable to the α,β-unsaturated lactam carbonyl, while the IR spectrum of **16** showed a band at 1599 and 1588 cm^{-1} assignable to the enamide group (angular-type). Linear and angular-type structures, **15** and **16,** were also clearly discernible by the ^{1}H and ^{13}C NMR spectra. The aromatic proton at the peri-position of product **15** appeared at δ 8.74, while the corresponding proton of product **16** appeared at δ 8.08, *ca.* 0.6 ppm upfield. The chemical shifts of the peri-protons of these products were parallel to those of the two types of furonaphthyridines, **14,** and **12a** and **12b,** respectively. The ^{13}C NMR Spectral data, which are based on the DEPT and ^{1}H-^{13}C COSY spectra, are given in Table 2. The signals due to the lactam carbonyl carbon and aromatic C(9) appeared at δ 161.4 and 131.6, 12.3 ppm and 3.6 ppm upfields of the corresponding signals of the linear-type isomer **12a.**

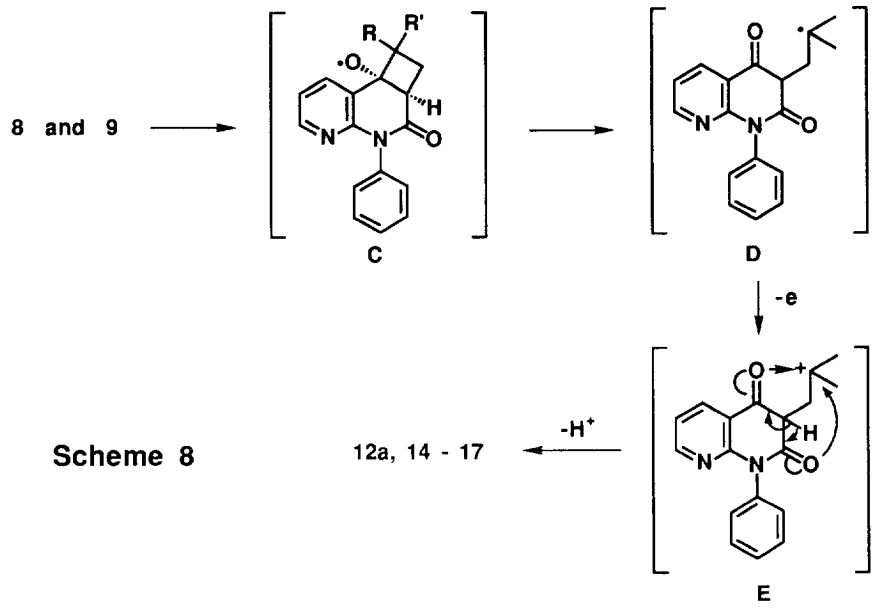
The photolysis of cyclobutanol **11** resulted in the formation of a single product **17** in 61% yield (Scheme 7). The molecular formula of product **17** was established to be $C_{21}H_{20}N_2O_3$ by combustion analysis and mass spectrometry. The IR spectrum, which exhibited a band at 1657 and 1587 cm^{-1} assignable to the enone group, and the ^{1}H NMR spectrum, which exhibited a signal at δ 8.11 assignable to the aromatic proton at the peri-position, indicated that the structure was (6bα,10aα)-(±)-6b,7,8,9,10,10b-hexahydro-10a-methoxy-5-phenylbenzofuro[3,2-*c*][1,8]naphthyridin-6(5*H*)-one **17**. A triplet signal at δ 3.43 (*J* 6.94 Hz) in the ^{1}H NMR spectrum is assignable to the 6β–H, and the 5/6 ring should be more stable *cis*-fused based on a steric consideration of the formation mechanism.

DISCUSSION

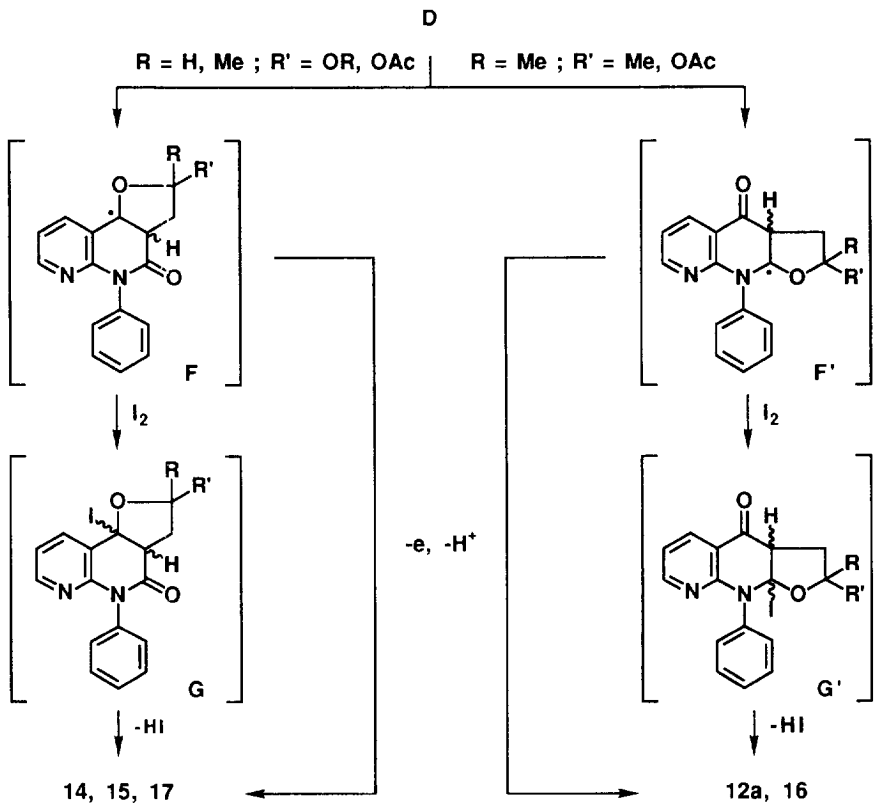
The Photoadditions of 4-*Hydroxy*-1-*phenyl* [1,8] *naphthyridin*-2(1H)-*one* **7** *with Electron-rich Alkenes* **2.** — The above-mentioned photoadditions of β–hydroxyenone chromophore incorporated in a heterocyclic molecule **7** to unsymmetrical alkenes **2** carrying electron-rich substituents invariably resulted in the formation of head-to-tail adducts, as in the case of the photoaddition of cyclohexenones.[7,8] The regioselectivity was also parallel to the photoaddition of α- or β–hydroxyenone chromophore incorporated in heterocyclic molecules , such as 3- or 4-hydroxycoumarin[3a,c] and 4-hydroxyquinolin-2(1*H*)-one.[3b]

The stereochemical outcome of the photoadditions of enone **7** with electron-rich alkenes was virtually parallel to those of 4-hydroxy-2 quinolone with alkenes previously reported by us;[3b] the photoaddition of 4-acetoxy-2-quinolone with 1-methoxycycloalkene afforded the *cis-transoid-cis* adduct exclusively,while the photoaddition with cycloalkene afforded *cis-cisoid-cis* adduct exclusively, or a mixture of *cis-cisoid-cis* and *cis-transoid-cis* adducts; the photoaddition of 4-acetoxy-2-quinolone with ethyl vinyl ether in methanol gave two isomeric head-to-tail photoadducts.

It should be noted that in contrast to the [2+2] photoadditions of cyclohexenone with electron-rich alkenes, which produced substantial quantities of 4/6 *trans*-fused photocycloadducts,[7,8] the [2+2] photoadditions of heteroaromatic enone **7** to alkene **2**,[3] including the present examples, invariably resulted in the exclusive formation of the thermodynamically more stable 4/6 *cis*–fused adducts. It is not clear at the present stage whether this difference in stereochemical outcome with the [2+2] photoaddition of cyclohexenones[7,8] was due to the different mechanisms in the two cases or whether the difference originated



Scheme 8



Scheme 9

from the greater strains in the twisted relaxed species and the 4/6 *trans*-fused adducts to be derived from the excited aromatic enones in the [2+2] photoadditions.

Paths leading to the Formation of Furonaphthyridinones **12a** *and* **14-17** *from the Hypoiodites of Cyclobutanols* **8, 9,** and **11** (*Schemes* 8 *and* 9).—— The foregoing results showed that cyclobutanols **8, 9** and **11**, derived from [2+2] photocycloaddition between 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1*H*)-one **7** and various alkenes **2,** gave furo[2,3-*b*][1,8]naphthyridin-4(2*H*)-ones, **12a** and **16** (the linear type), and/or furo[3,2-*c*][1,8]naphthyridin-4(2*H*)-ones, **14, 15,** and **17** (the angular type), when their benzene solutions containing 3 equiv. each of mercury(II) oxide and iodine were irradiated with Pyrex-filtered light.

The probable paths giving rise to the furonaphthyridinones from the hypoiodites of the cyclobutanols **8,9,** and **11** are outlined in Schemes 8 and 9. These paths are essentially parallel to those leading to the formation of the furochromones, furocoumarins and furoquinolinones from the cycloadducts of 4-hydroxycoumarin [3a] and 4-hydroxy-2-quinolone.[3b]

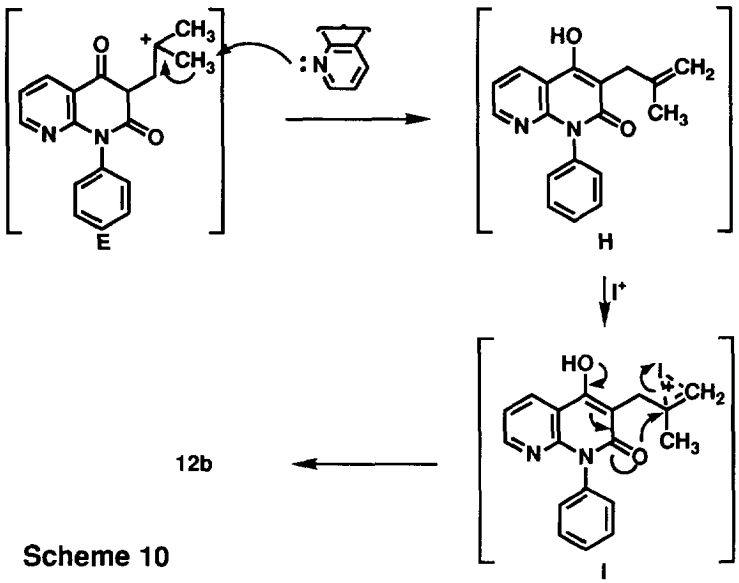
Thus, the alkoxyl radical **C** generated from the cyclobutanol hypoiodites gives carbon-centred radical **D,** arising from the selective β–scission of their non-ring junction bond (Scheme 8). There seems to be two probable paths leading to the formation of furonaphthyridinones from the radical **D.** In the first mechanism, furonaphthyridinones **12a, 14-17** may be formed by the cyclization of an ionic intermediate **E** generated from a one-electron oxidation of the carbon-centred radical **D** (as outlined in Scheme 8).

Alternatively, the furonaphthyridinones can be formed *via* a radical cyclization (as outlined in Scheme 9); an intramolecular combination of carbon-centred radical **D** with either oxygen of the two carbonyls forms cyclic radicals **F** and **F'** from which furonaphthyridinones **12a, 14-17** are formed through iodides **G** and **G'** or through a one-electron oxidation followed by the loss of a proton, (as outlined in Scheme 9). Of these paths, the formation of an iodide corresponding to the hypothetical intermediates **G** and **G'** has been reported in the photolysis of widdrol hypoiodite.[9]

As in the case of the photolysis of the hypoiodites of the cyclobutanols derived from the cycloaddition of 4-hydroxycoumarin and 4-hydroxy-2-quinolone, the hypoiodites of cyclobutanols **8, 9** and **11** again resulted in the formation of linear- (**12a, 12b**, and **16**) and/or angular-type furonaphthyridinones (**14, 15**, and **17**). The selectivity of the formation of the two types of products including byproduct **12a** was parallel to those in the photolysis of the quinolone series previously reported.[2b] Thus, the angular-type products were exclusively formed in the photolysis of cyclobutanol adducts carrying an alkoxyl group on the cyclobutane ring, while the linear- type products were exclusive products in the photolysis of cyclobutanol adducts carrying alkyl groups on the cyclobutane ring. The directing effects of the acetoxyl group were again not as powerful as those of the alkoxyl and alkyl groups, and both angular and linear furonaphthyridinones were formed when the cyclobutanol hypoiodite carrying the acetoxy group on the cyclobutane ring was irradiated. Thus, the replacements of C(5) and 4-Me of 4-methylcyclobuta[*c*]quinolin-3(1*H*)-one by a nitrogen and a phenyl group, respectively, did not affect the selectivity for the formation of the two types of furonaphthyridinones.

A Mechanism of The Formation of Byproduct **12b.**——A probable mechanism for the formation of a byproduct **12b**, which was not produced in the photolysis of the quinolinone series, is outlined in Scheme 10. It is probably formed through an intermediate alkene **H** produced by removing a proton from the cationic

intermediate **E'** with a base. An intramolecular reaction of an iodonium ion generated from the alkene **H** may give product **12b.** It would be possible that a naphthyridinone, which is more basic than quinolinones, acted as the base.



Scheme 10

EXPERIMENTAL

M.p.s were determined with a Yanagimoto micro m.p. apparatus, and are uncorrected. The IR spectra were determined for Nujol mulls with a JASCO IR 810 infrared spectrometer. The ^{1}H and ^{13}C NMR spectra were determined in $CDCl_3$ ($SiMe_4$ as internal reference) with a JEOL JNM-EX 270 spectrometer operating at 270 MHz. High- and low-resolution mass spectra were recorded with a JEOL JMS-DX 303 or a JMS-HX 110. The UV spectrum was recorded with a JASCO Ubest-30 UV/VIS spectrophotometer. PLC was carried out on a Merck Kieselgel 60 PF_{254}. The [2+2] photocycloadditions were carried out with a 500-W High-pressure Hg arc lamp (Eikosha EHB-WI-500). The photolysis of the hypoiodites was carried out with a 100-W high-pressure Hg arc lamp (Eikosha EHB-WU-100).

***4-Hydroxy-1-phenyl*[1,8]*naphthyridin*-2(1H)-*one* 7.**——This compound was prepared from 2-chloronicotic acid according to the procedure of Sherlock et al.[5] 7; λ_{max} (MeOH) / nm : 314 nm (ε : 12600) (2.40×10^{-5} mol/l).

[2+2] *Photocycloaddition of* 4-*Hydroxy*-1-*phenyl*[1,8]*naphthyridin*-2(1*H*)-*one* 7.

(i) *With Isobutene* 2a.——A solution of 4-hydroxy-1-phenyl[1,8]naphthyridin-2(1*H*)-one **7** (150 mg, 0.63 mmol) and isobutene **2a** (1.8 g, 32.1 mmol) in MeOH (71 cm^3) was irradiated through a Pyrex-filter with a 500-W high-pressure Hg arc under nitrogen for 15h at room temperature. Evaporation of the solvent gave a

crude product, which was purified by PLC on silica gel [EtOAc/hexane ; 3/1] to give cyclobutanol **8a**, (2aα, 8bα)-(±)-2,2a,4,8b-tetrahydro-8b-hydroxy-1,1-dimethyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8a** (170 mg, 95 %). m.p. 203-205°C (from EtOAc); (Found: C, 73.45; H, 6.13; N, 9.43. $C_{18}H_{18}N_2O_2$ requires C, 73.45; H, 6.16; N, 9.52 %); δ_H 0.93 (3H,.s, Me), 1.41 (3H, s, Me), 1.65 (1H, dd, *J* 9.57 and 11.22, 2-H), 2.24 (1H,.dd, *J* 10.22 and 11.22, 2-H), 2.70 (1H, br.s, OH), 3.58 (1H, dd, *J* 9.57 and 10.22, 2a-H), 7.03 (1H,.dd, *J* 4.62 and 7.59, 7-H), 7.17 (2H,.br.d, *J* 6.93, Ph), 7.38-7.56 (3H, m, Ph), 7.74 (1H,.dd, *J* 1.98 and 7.59, 8-H), 8.21 (1H, dd, *J* 1.98 and 4.62, 6-H); ν_{max}/cm^{-1} 3336, 1666; *m/z* (FD) 294 (M^+, 29), 238 [(M-C_4H_8)$^+$, 100].

(ii) ***With Ethyl Vinyl Ether*** **2b.** ——A solution of naphthyridinone **7** (50 mg, 0.21mmol) and ethyl vinyl ether **2b** (1.0 cm^3, 10.5 mmol) in MeOH (23.6 cm^3) was irradiated for 3h as described above. Evaporation of the solvent gave a mixture of products which was separated by PLC on silica gel [EtOAc/hexane ; 3/1] to give a more mobile fraction, (1α,2aα,8bα)-(±)-1-ethoxy-2,2a,4,8b-tetrahydro-8b-hydroxy-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one **8b** (24 mg, 37 %) and a less mobile fraction, (1α,2aβ,8bβ)-isomer **9b** (28 mg, 43 %).

8b; m.p. 166-168°C(from EtOAc); (Found: C, 69.48; H, 5.87; N, 8.96. $C_{18}H_{18}N_2O_3$ requires C, 69.66 ; H, 5.85; N, 9.03 %); δ_H 1.30 (3H,.t, *J* 6.93, Me), 2.27 (1H,.ddd, *J* 5.94, 7.92 and 12.86, 2-H), 2.52 (1H,.ddd, *J* 2.97, 10.89 and 12.86 Hz, 2-H), 3.58 (3H,.m, OCH_2 and 2a-H), 4.07 (1H,.ddd, *J* 0.99, 2.97 and 5.94, 1-H), 4.18 (1H,.br.s, OH), 7.04 (1H,.dd, *J* 4.62 and 7.58, 7-H), 7.19 (2H,.br.d, *J* 7.43, Ph), 7.38-7.54 (3H, m, Ph), 7.84 (1H, dd, *J* 1.98 and 7.58, 8-H), 8.20 (1H,.dd, *J* 1.98 and 4.62, 6-H); ν_{max}/cm^{-1} 3450 (OH), 1676 (C=O); *m/z* (EI) 310 (M^+, 1.8), 281 [(M-Et)$^+$, 2.2], 264 [(M-EtOH)$^+$, 1.3], 251 (0.99), 237 [(M-CH_2CH_2OEt)$^+$, 100].

9b; m.p. 189-191°C (from AcOEt); (Found: C, 69.58; H, 5.93; N, 9.13. $C_{18}H_{18}N_2O_3$ requires C, 69.66 H, 5.85; N, 9.03 %); δ_H 1.18 (3H,.t, *J* 6.93, Me), 1.57 (1H, dt, *J* 9.24 and 10.55, 2-H), 2.52 (1H,.ddd, *J* 7.92, 9.24 and 10.55, 2-H), 3.03 (1H,.dd, *J* 9.24 and 10.55, 2a-H), 3.51 (1H, br.s, OH), 3.53-3.72 (2H,.m, OCH_2), 4.14 (1H,.dd, *J* 7.92 and 10.55, 1-H), 7.04 (1H, dd, *J* 4.95 and 7.59, 7-H), 7.12 (2H, br.d, *J* 7.26, Ph), 7.35-7.55 (3H,.m, Ph), 7.85 (1H, dd, *J* 1.98 and 7.59, 8-H), 8.21 (1H,.dd, *J* 1.98 and 4.95, 6-H); ν_{max}/cm^{-1} 3406 (OH), 1672 (C=O); *m/z* (EI) 310 (M^+, 0.83), 281 [(M-Et)$^+$, 2.2], 264 [(M-EtOH)$^+$, 1.1], 251 (0.9), 237 [(M-CH_2CH_2OEt)$^+$, 100].

(iii) ***With Isopropenyl Acetate*** **2c.**—— A solution of naphthyridine **7** (100 mg, 0.42 mmol) and isopropenyl acetate **2c** (2.3 cm^3, 20.99 mmol) in MeOH (47.2 cm^3) was irradiated for 6h in a similer manner as mentioned above. After evaporation of the solvent, the crude product was purified by PLC on silica gel [hexane/EtOAc ; 1/3] to give a product **8c** or **9c** (108.8 mg, 76.6 %), (2aα,8bα)-(±)-1-acetoxy-2,2a,4,8b-tetrahydro-8b-hydroxy-1-methyl-4-phenylcyclobuta[*c*][1,8]naphthyridin-3(1*H*)-one. m.p. 263-264°C (from MeOH); (Found: C, 67.43; H, 5.35; N, 8.32. $C_{19}H_{18}N_2O_4$ requires C, 67.44 ; H, 5.37; N, 8.32 %); δ_H 1.75 (s, 3H, Me), 1.85 (3H,.s, MeCOO-), 2.06 (1H,.t, *J* 11.22, 2-H), 2.78 (1H,.dd, *J* 9.57 and 11.22, 2-H), 3.07 (1H, s, OH), 3.25 (1H,.dd, *J* 9.57 and 11.22, 2a-H), 7.05 (1H,.dd, *J* 4.62 and 7.76, 7-H), 7.15 (2H,.br.d, *J* 6.93, Ph), 7.25-7.53 (3H,.m, Ph), 7.92 (1H,.dd, *J* 1.98 and 7.76, 8-H), 8.24 (1H,.dd, *J* 1.98 and 4.62, 6-H); ν_{max}/cm^{-1} 3434 (OH), 1732 (OC=O), 1673 (C=O); *m/z* (EI) 338 (M^+, 0.57), 277 (51.3), 237 [(M-$C_2H_3CH_3OAc$)$^+$, 100].

(iv) ***With* 1-*Methoxy-1-cyclohexene*** **10**.[6]——Irradiation of a solution of naphthyridine **7** (100 mg, 0.42 mmol) and 1-methoxy-1-cyclohexene **10** (2.6 cm^3) in MeOH (47.2 cm^3) was carried out in a similar manner as above for 3h. After evaporation of the solvent, a residue was separated by PLC on silica gel [CH_2Cl_2/MeOH ; 80/1, 50/1 × 2] to give (6aα,6bβ,10aβ,10bα)-(±)-6a,6b,7,8,9,10,10a,10b-octahydro-10b-hydroxy-10a-methoxy-5-phenylbenzo[3,4]cyclobuta[1,2-*c*][1,8]-naphthyridin-6(5*H*)-one **11** (73.2 mg, 49.8 %) and a mixture (39.1 mg) including (6aα,6bα,10aα,10bα)-isomer (by ^1H NMR).

11; m.p. 236.5-238°C ($CHCl_3$); (Found. C, 56.28; H, 4.99; N, 6.02; Cl, 22.56. $C_{21}H_{22}N_2O_3 \cdot CHCl_3$ requires C, 56.24; H, 4.94; N, 5.96; Cl, 22.64 %); δ_H (DMSO-d_6) 1.23-1.33 (1H,.m), 1.51-1.57 (m, 2H), 1.72-1.84 (3H,.m), 2.13-2.20 (2H, m,), 2.25 (1H,.dd, *J* 4.62 and 10.56, 6b-H), 3.03 (1H,.d, *J* 10.56, 6a-H), 3.17 (3H, s,.OMe), 7.02 (1H, dd, *J* 4.62 and 7.76, 1-H), 7.18 (2H, br.d, *J* 7.26, Ph), 7.37-7.53 (4H,.m, Ph and $CHCl_3$), 7.93 (1H, dd, *J* 1.98 and 7.76, 2-H), 8.16 (1H, dd, *J* 1.98 and 4.62, 3-H); ν_{max}/cm^{-1} 3364, 1663; *m/z* (FD) 351[$(MH)^+$, 100], 238[$(M\text{-}C_6H_{10}OMe)^+$, 40.9].

General Procedure for the Photolysis of the Hypoiodite of Cyclobutanols.——To a solution of a cyclobutanol in benzene (0.02 M), mercury(II) oxide (2 equivalents) and iodine (2 equivalents) were added. The solution was flushed with nitrogen and then irradiated with a 100 W high-pressure Hg arc through a Pyrex-filter at room temperature. The reaction mixture was filtered through Celite and the organic layer was washed successively with 5 % $Na_2S_2O_3$ solution, water, and saturated brine. After dryness over anhydrous Na_2SO_4 and evaporation of the solvent, the crude product was subjected to PLC to give pure products.

Photolysis of the Hypoiodite of Cyclobutanol **8a**.——Cyclobutanol **8a** (130 mg, 0.44 mmol) in benzene (22 cm^3) containing mercury(II) oxide (287.3 mg, 1.32 mmol) and iodine (336.4 mg, 1.32 mmol) was irradiated for 5h. After usual workup, the crude products were subjected to PLC on silica gel [EtOAc/hexane ; 5/1, 7/1, 10/1 × 2] to give three fractions. The most mobile fraction was a recovered starting cyclobutanol **8a** (16 mg, 12.3 %). The next mobile fraction (41 mg, 22.2 %) was 3,9-dihydro-2-iodomethyl-2-methyl-9-phenylfuro[2,3-*b*][1,8]naphthyridin-4(2*H*)-one **12b**. m.p. 168.5-170°C (from acetone); (Found C, 51.88; H, 3.64; N, 6.33; I, 30.12. $C_{18}H_{15}N_2O_2I$ requires C, 51.69; H, 3.62; N, 6.70; I, 30.34 %); δ_H 1.70 (s, 3H, Me), 3.29 (1H, d, *J* 14.52, 3-H), 3.38 (3H, d, *J* 14.52, 3-H), 3.42 (1H, d, *J* 10.88 Hz, $C\underline{H}_2I$), 3.48 (1H, d, *J* 10.88, $C\underline{H}_2I$), 7.26-7.58 (6H, m, 6H, Ph and 6-H), 8.52 (1H, dd, *J* 1.98 and 4.62, 7-H), 8.74 (1H, dd, *J* 1.98 and 7.91, 5-H); ν_{max}/cm^{-1} 1623, 1591; *m/z* (FD) 418 (M^+, 100).

The most polar fraction (54.7 mg, 42.4 %) was 3,9-dihydro-2,2-dimethyl-9-phenylfuro[2,3-*b*][1,8]-naphthyridin-4(2*H*)-one **12a** (54.7 mg, 42.4 %). m.p. 193-195.5°C (from EtOAc); (Found C, 74.10; H, 5.70; N, 9.51. $C_{18}H_{16}N_2O_2$ requires C, 73.95; H, 5.52; N, 9.58 %); δ_H 1.52 (6H, s, Me × 2), 3.13 (2H, s, 3-H), 7.26-7.36 (3H, m, 6-H and Ph), 7.52-7.61 (3H, m, Ph), 8.50 (1H, dd, *J* 1.98 and 4.62, 7-H), 8.74 (1H, dd, *J* 1.98 and 7.75, 5-H); ν_{max}/cm^{-1} 1611, 1592; *m/z* (FD) 292 (M^+, 100), 284 (18.68).

The yields of **12a** and **12b** based on the converted cyclobutanol were 48.3 % and 25.3 %.

Photolysis of the Hypoiodite of Cyclobutanol **8b**.——Cyclobutanol **8b** (50 mg, 0.16 mmol) in benzene (8.5 cm^3) containing mercury(II) oxide (110.5 mg, 0.48 mmol) and iodine (129.4 mg, 0.48 mmol) was irradiated for 5h. After usual workup, the crude products were subjected to PLC on silica gel [acetone/hexane ; 1/1] to give two fractions. The more mobile fraction (15.4 mg, 31 %) was (±)-2-ethoxy-3,5-dihydro-5-